may be warranted to discern if DM pts may benefit from different methods of mobilization or if long term transplant outcomes are impacted.

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Hematopoietic Cell Transplantation (HCT)-Specific Comorbidity Index in Autologous Stem Cell Transplant Indicates People with Advanced Age and Increased Comorbidity Index Should be Hosptialized Through Engraftment

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The hematopoietic cell transplantation specific comorbidity index (HCT-CI) has been proven to be a valuable tool in allogeneic stem cell transplant (ASCT) recipients to predict overall survival. There are few studies that use the HCT-CI for evaluating autologous stem cell transplantation. Our institution performs autologous stem cell transplants in a variety of settings, from completing the whole transplant process inpatient to instituting their preparative regimen through transplant and engraftment in the outpatient setting. We retrospectively reviewed our experience of 250 autologous stem cell transplants who had a diagnosis that included Multiple Myeloma, Non-Hodgkin's Lymphoma, Hodgkin's Lymphoma, and Testicular Carcinoma that were either treated inpatient for their hospital course or were prepared in the outpatient setting and/or were discharged very early in their transplant course (day-1 or within three days of their autologous transplant). The median age of the inpatient transplant group was 63.5 compared to the outpatient group that was 58, $P < 0.006$. The average comorbidity index for the inpatient group was 2.086 compared to the outpatient group 1.23, $P < 0.001$. In conclusion, our institution, using the HCT-CI and age for autologous stem cell transplantation helps to identify those candidates that are more successfully treated in the inpatient setting and the outpatient setting. This study was limited by its retrospective nature, small size and single center experience. Prospective randomized studies are needed to determine whether or not the HCT-CI in autologous stem cell transplantation is truly effective.

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Autologous Hematopoietic Stem Cell Transplant (aHSCT) is a Safe and Reasonable Treatment in Patients with Primary Systemic Amyloidosis (AL amyloidosis)

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Background: There is no current standard of care for patients with newly diagnosed AL amyloidosis. Autologous HSCT is a potential option, but has been limited in its use due to increasd treatment-related mortality (TRM) (38% from one randomized study). Two large retrospective analyses showed improved overall survival (OS) (70% at 4 yrs and 47% at 5 yrs) of AL amyloid patients undergoing aHSCT compared to control (40% at 4 yrs) with TRM of 13%.

Methods: We retrospectively analyzed the outcomes of 29 newly diagnosed AL amyloidosis patients who underwent aHSCT between 10/1998 and 5/2012. Hematologic responses were evaluated, along with post-transplant survival and TRM. Progression-free survival (PFS) and (OS) were determined using the Kaplan-Meier method.

Results: Of the patients transplanted, 13 were female and 16 were male. Median age at aHSCT was 56 (range 26-71). Eleven (38%) had involvement of at least 2 organs. Median brain natriuretic peptide and troponin available in 20 patients were 109 pm/ml (range 24-502) and 0.02ng/ml (range 0.01-1.17). Twenty-one patients (72%) received high dose Melphalan 200 mg/m^2. Median CD34+ infused stem cells was 5.00 x 10^6/kg. No patients received filgrastim or other colony stimulating factor. Time to neutrophil and platelet engraftment were 12 and 17 days, respectively. Three months hematologic response was available in 22 patients and showed complete response, partial response, and stable disease in 15(68%), 2 (10%) and 5(22%), respectively. The 1, 3, and 5 year PFS were 78%, 68% and 41%, respectively. One, 3, and 5 year OS from diagnosis and from aHSCT were 81, 66, and 66% and 89, 66 and 66% respectively (Table 1). The 100-day and 1 year TRM were 3.4% (1 patient) and 6.9% (2 patients), respectively.

Conclusion: Our results show that autologous HSCT is a reasonable option for patients with newly diagnosed AL amyloidosis. The 100 day and 1 year TRM compares favorably to multiple myeloma patients undergoing autologous HSCT.

Table 1

	N	Censored	1 yr survival rate (%)	3 yr survival rate (%)	5 yr survival rate (%)	Median (months)	95% CL (months)
PFS	29	18	78	68	41	44.7	(17.3, NA)
OS-HSCT	29	20	81	66	66	112.0	(13.9, NA)
OS-DX	29	20	89	66	66	117.2	(18.7, NA)

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Safety and Efficacy From Intravenous Busulfan with PK-Directed Dosed Adjustment and Bortezomib Conditioning Regimen in Relapsed Multiple Myeloma Patients Undergoing a Second Autologous Hematopoietic Stem Cell Transplantation

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The aim of this prospective, multicenter Phase IIa study was to investigate whether daily intravenous busulfan (IV Bu) with bortezomib is a safe and effective conditioning regimen prior to second, salvage autologous hematopoietic stem cell transplantation (ASCT) for relapsed multiple myeloma (MM) patients.

Thirty patients with relapsed MM were enrolled at 11 centers in the US and Canada. Median age at second ASCT was 59 years (range: 48-73). Median time from first ASCT to second ASCT was 28.0 months (range: 12-119). At the time of second ASCT, 7 (23.3%) patients were in very good partial response (VGPR), 12 (40.0%) in partial response (PR), 2 (6.7%) in stable disease (SD), and 9 (30.0%) in progressive disease (PD).

Patients received a test IV Bu dose (0.8 mg/kg) over 2 hours between Days -12 and -9. The test PK dosing was based on adjusted ideal body weight (AIBW= ideal BW + 0.25 [actual BW − ideal BW]) for all patients except for those whose actual BW is less than or equal to the ideal BW. For those subjects, actual BW was used. Pharmacokinetic (PK) analysis determined Bu exposure as area under the concentration-time curve (AUC), and provided optimized doses so that a total target AUC would achieve 20,000 mMmin. These optimized doses were administered over 3 hours, once daily from Day -5 to Day -2. Confirmatory PK was conducted on Day -5; Bu doses were further adjusted on Days -3 and -2, if needed. Bortezomib (1.3 mg/m^2) was intravenously administered on Day -1.

The most common grade 3 or 4 adverse events (CTCAE v3.0) were febrile neutropenia (50.0%), stomatitis (43.3%), and nausea (13.3%). One transplant-related death occurred due to pulmonary complications in a patient with Parkinson's disease on Day 20. There were no reported instances of seizure, worsening neuropathy, or hepatic veno-occlusive disease meeting the Baltimore criteria.

Post-transplant disease response using the 2006 IMWG criteria was available for 28 patients. At 3 months, there were 2 (6.7%) CR, 5 (16.7%) VGPR, 4 (13.3%) PR, 8 (26.7%) SD, and 9 (30.0%) PD. At 6 months, there was 1 (3.3%) stringent CR, 1 (3.3%) CR, 4 (13.3%) VGPR, 7 (23.3%) SD, and 14 (46.7%) PD. Median progression-free survival was 191 days, while median overall survival was not reached.

Test PK showed that 40.0% (n=12/30) of patients had AUC <1,000 (n=11) and AUC >1,500 μM*min (n=1). If body weight-based doses had been used *without test PK*, these patients (40%) would have been dosed outside the target total AUC range (>24,000 or < 16, 000 μM*min) for conditioning. The confirmatory PK on Day -5 revealed that a total AUC fell within the target range in 28 patients (93.3%), while two (6.7%) needed dose reduction on Days -3 and -2.
In conclusion, a combination of IV Bu and bortezomib prior to second ASCT had acceptable safety profile and induced 20% VGPR or better responses at 6 months. No cases of VOD were observed in this group of patients in whom dose optimization using pre-transplant test PK was utilized.

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Delayed Neutrophil Engraftment Associated with Early CD 8 Polyclonal Lymphocyte Recovery Post Autologous Stem Cell Transplant for Multiple Myeloma

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Delayed engraftment following high-dose chemotherapy and autologous peripheral stem cell transplantation is a rare event. Here, we report two cases of delayed engraftment following autologous peripheral blood stem cell transplant (PBSCT) for Multiple Myeloma (MM) associated with early recovery of polyclonal lymphocytes and response to steroids. Both of our patients were 51 years old at time of transplant and women. The preparative regimen consisted of Melphalan 200mg/m2 prior to stem cell infusion; the stem cell doses were between 2.5 and 2.8 million per kilogram. Per protocol, each received growth factor beginning at day 5 post-transplant. Both patients demonstrated a relative increase in their peripheral blood lymphocyte count without neutrophil recovery by day 15 in one patient and day 25 post-transplant in the other. Peripheral blood for flow cytometry was negative for lymphoproliferative disorder or recurrence of their disease. However, it was noted that their CD4:CD8 ratio was 1:6.5 and 1:6.3 with marked increase in CD8 lymphoctyes. This expansion of CD8+ cells has been implicated in autoimmune cytopenias in patients with autoimmune diseases and was thought to be the cause of cytopenias in our patients. Given the delay in neutrophil recovery, prednisone 1mg/kg was started for concerns that the predominantly CD 8 polyclonal lymphocytes were responsible for suppressing hematopoiesis. Within 48-72 hours of starting steroids, the peripheral blood lymphocytes decreased significantly, and both patients demonstrated neutrophil engraftment followed by platelet engraftment in the subsequent two-week period. Delayed engraftment following autologous PBSCT is uncommon. Viral infection is a common etiology, and rarely, lymphoproliferative processes like large granular lymphocytes (LGL) have been reported post high-dose therapy and autologous PBSCT for MM. In our patients, no viral cause was found and there was no clonal lymphocyte population. In conclusion, this is the first report of post autologous PBSCT delayed engraftment in association with a predominantly CD 8 polyclonal lymphocyte population. This process was readily reversible with corticosteroid therapy and did not necessitate re-transplantation.

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Evaluating the Effect of High Dose Chemotherapy and Autologous Bone Marrow Transplantation (ASCT) on Hypertension (HTN) in Multiple Myeloma (MM) Patients

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Background: A recent study showed that ASCT may reverse kidney failure in one third of multiple myeloma patients, which can lead to improvement in blood pressure. However, there is very limited published data studying the impact of the treatment on blood pressure control.
Methods: We conducted a review of electronic medical records of 184 patients with established diagnosis of MM that underwent an ASCT at Karmanos Cancer Institute between January 1st, 2009 and December 31st, 2010. We